Exhibit 7

Establishment Inspection Report FEI: **3008903511**

Hetero USA Inc EI Start: 3/7/2017

Piscataway, NJ 08854-4124 EI End: 3/17/2017

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SUMMARY

This Postmarketing Adverse Drug Experience (PADE) inspection was conducted at the pharmaceutical US corporate headquarters of Hetero. This inspection was initiated as per request from CDER, Office of Compliance, FACTS Assignment # 11681700, FACTS OP ID # 8866258, MARCS OP ID # 43453. Guidance for the inspection was provided by Compliance Program 7353.001: Postmarketing Adverse Drug Experience (PADE) Reporting Inspection and CP 7356.021 Drug Quality Reporting System (DQRS) (MedWatch Reports); NDA Field Alert Reports (FARs).

The previous inspection was conducted from 07/19/2011 to 07/20/2011 and provided limited coverage for a complaint investigation review of DQRS report 2011-03485 Torsemide Tablets 100 mg, lot E100688. An FDA 483, Inspectional Observations was issued on 07/20/2011 due to failure to file a Field Alert Report within three (3) business days.

The current inspection covered PADE operations handled by the firm, which includes the receipt and submission of postmarketing adverse drug experience periodic reports (PADERs), regulatory documents and annual reports, complaint handling, submission of Field Alert Reports (FARs) and receipt of DQRS reports. An inspectional closeout meeting was held with the firm’s management team on 03/17/2017. An FDA 483, Inspectional Observations was issued to Mr. Seshu Akula, Executive Vice President, due to failure to submit PADERS within 30 days of the close of the quarter, written procedures not being developed for receipt and reporting of PADE activities, and failure to submit PADERs in electronic format.

No samples were collected and no refusals were encountered.

ADMINISTRATIVE DATA

Inspected firm:	Hetero USA Inc
Location:	1035 Centennial Ave Piscataway, NJ 08854-4124
Phone:	-
FAX:	-
Mailing address:	1035 Centennial Ave, Piscataway, NJ 08854-4124
Dates of inspection:	3/7/2017-3/8/2017 , 3/10/2017, 3/13/2017, 3/16/2017-3/17/2017
Days in the facility:	6
Participants:	**Guerlain Ulysse, Investigator** **Tonia F Bernard, Investigator**

On 03/07/2017, we, Investigators Guerlain Ulysse and Tonia Bernard, presented our credentials and issued a Form FDA 482, Notice of Inspection (**Attachment 2**) to Dr. Soma Ragu, Director of Regulatory Affairs. Dr. Ragu stated that he was authorized by Mr. Seshu Akula, Executive Vice President, to receive notice of inspection. Mr. Akula was not present at the beginning of the inspection. Later during inspection, Dr. Ragu, Director of Regulatory Affairs also informed us that the name “Indukuri” is a part of his surname. Thus, his complete name and title is: Dr. Soma Ragu Indukuri, Director of Regulatory Affairs. On 03/17/2017, an inspectional closeout meeting and verbal discussion was held with management and an FDA-483, Inspectional Observations, was issued due to failure to submit PADERS within 30 days of the close of the quarter, written procedures not being developed for receipt and reporting of PADE activities, and failure to submit PADERs in electronic format (**Attachment 1**).

This inspectional report was written by Investigator Guerlain Ulysse.

Investigator Ulysse was present all days of the inspection. Investigator Bernard was present on 03/07/2017, 03/08/2017, and 03/10/2017.

Post-inspectional correspondence should be addressed to:
Seshu S. Akula, Executive Vice President
Hetero USA, Inc.
1035 Centennial Ave.
Piscataway, NJ 08854
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HISTORY

Hetero USA, Inc., Piscataway, NJ is the US corporate headquarters for Hetero, which is the firm's parent company composed of Hetero Drugs Limited and Hetero Labs Limited, Unit III and V, Hyderabad, India (**Exhibit 1, Page 3**). Hetero originated from Hetero Drugs Limited, which is an Indian Pharmaceutical Company established in the year 1993 by Dr. Bandi Parthasaradhi Reddy; the parent company is responsible developing, manufacturing, and marketing active pharmaceutical ingredients (APIs), intermediate chemicals, and generic finished dosages.

Hetero USA, Inc. was established in 2010 and reports to Hetero Labs Limited, Unit III and V, which is the generic pharmaceutical company division of Hetero (**Exhibit 2**). According to Dr. Ragu Indukuri, Director of Regulatory Affairs, all abbreviated new drug applications (ANDAs) are filed under Hetero Labs Limited Unit-III and Unit-V. The firm provided at list of currently approved drug products (**Exhibit 3**), a list of pending ANDAs (**Exhibit 4**), and a list of withdrawn ANDAs since the previous inspection (**Exhibit 5**). According to Dr. Ragu Indukuri, Director of Regulatory Affairs, Hetero Drugs Limited is primarily responsible for developing and marketing APIs and intermediate chemicals. Hetero has approximately twenty other subsidiary sites around the rule. The two US subsidiaries include:

- Hetero USA Inc., 1035 Centennial Ave, Piscataway, NJ, which is the US Corporate Headquarters for Hetero Labs Ltd and Hetero Drug Ltd, India. According to established agreements, Hetero USA is responsible for ANDA submissions, periodic report submissions, amendments, annual reports and any other submissions sent to the FDA on behalf of the parent company (**Exhibit 6**).
- Camber Pharmaceuticals Inc., 1031 Centennial Ave, Piscataway, NJ, which is the pharmaceutical distributor and label brand name for generic finished dosages products manufactured by Hetero Labs Ltd, India. Hetero USA Inc. is responsible for handling customer complaints, product recalls, training, and scientific and regulatory affairs activities on behalf of Camber Pharmaceuticals, Inc. (**Exhibit 7**).

According to Dr. Ragu Indukuri, Director of Regulatory Affairs, InvaGen Pharmaceuticals Inc., Hauppauge, NY, a previous subsidiary and pharmaceutical distributor for Hetero Drug Limited, was sold to Cipla Pharmaceuticals in February 2016.

The firm is composed of administrative offices and is approximately (b) (4) square foot. The firm currently employs approximately (b) (4) full-time employees and operates (b) (4) (b) (4) . According to Mr. Ragu Indukuri, Director of Regulatory Affairs, 2016 gross annual sales for Hetero US marketed products was approximately (b) (4) .

INTERSTATE (I.S.) COMMERCE

Hetero USA Inc., is responsible for US regulatory and certain PADE activities for ANDAs filed by Hetero Labs Ltd., India. The generic drug products are marketed and distributed under the Camber Pharmaceuticals Inc. label brand name. All finished drug products are manufactured and received from Hetero Labs Ltd, Unit III and V. According to the firm, approximately(b) (4)% of the firm's US drug products are distributed outside of the state of New Jersey. In addition, approximately(b) (4)% of drug products are distributed to wholesalers. Some of the firm top customers includes:

(b) (4)	

JURISDICTION (PRODUCTS MANUFACTURED AND/OR DISTRIBUTED)
The firm is the US corporate headquarters for Hetero, which is composed of Hetero Labs Ltd., India and Hetero Drugs Ltd., India, and is responsible for submitting and handling US regulatory documents, PADERs, and complaints received by Camber Pharmaceuticals Inc.

The firm's top five products by volume include:

(b) (4)

The firm's top three products by sales include:

(b) (4)

These drug products are supplied to the market via interstate and are subject to the Food, Drug, and Cosmetic Act.

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED
The following individuals participated in the current inspection. An organizational chart was provided by the firm (**Exhibit 8**).

Mr. Seshu S. Akula, Executive Vice President, is the most responsible individual at the firm and is responsible for overseeing marketing, business, and regulatory activities at Hetero USA, Inc. Mr.

Akula was not present at the beginning of the inspection to receive the Form FDA-482, Notice of Inspection. Mr. Akula was present at the inspectional closeout meeting and was issued the Form FDA-483, Inspectional Observations. Mr. Akula reports directly to Dr. Bandi Parthasaradhi Reddy, Chairman & Managing Director of Hetero Inc. located in Hyderabad, India.

Dr. Soma Ragu Indukuri, Director of Regulatory Affairs, is responsible for overseeing all US regulatory activities for Hetero Labs Ltd and Camber Pharmaceuticals, Inc. Dr. Ragu Indukuri is the US Agent for products distributed by Camber Pharmaceuticals, Inc. He is also responsible for reviewing regulatory activities involving ANDA submissions, Field Alert Reporting (FAR), product recalls, and submission of postmarketing periodic reports. Dr. Ragu Indukuri reports directly to Mr. Seshu Akula, Executive Vice President.

Mr. Raghunath Chigurupati, Manager of Regulatory Affairs, is responsible for coordinating regulatory affairs activities, handling, evaluating, and forwarding market and PV complaints to support Camber Pharmaceuticals, reviewing submission of annual reports, and completing regulatory projects. Mr. Chigurupati reports directly to Dr. Ragu Indukuri, Director of Regulatory Affairs.

Mr. Rajesh Kankula Manager of Regulatory Affairs, is responsible for analyzing and preparing regulation submissions, ensuring timely completion of regulatory projects, reviewing and submitting annual reports. Mr. Kankula is also responsible for reviewing labeling, advertising, and promotional labeling to ensure compliance, and preparing ANDA documents and submissions. Mr. Kankula reports directly to Dr. Ragu Indukuri, Director of Regulatory Affairs.

Via Teleconference:

Dr. Souvik Chattergee, Assistant General Manager (AGM) of Hetero PV Department, Hyderabad, India. Dr. Chattergee is responsible for overseeing pharmacovigilance activities at Hetero, Hyderabad, India. Dr. Chattergee assisted in forwarding relevant PV and PADE documents to Dr. Ragu Indukuri, Director of Regulatory Affairs for our review. Dr. Chattergee reports to Dr. SD Sinha, VP and Head of Global Pharmacovigilance, Clinical Development, and Medical Affairs located at Hetero, Hyderabad, India (**Exhibit 9**).

FIRM'S TRAINING PROGRAM

The regulatory affairs department of Hetero USA is responsible for receiving, mailing and submitting periodic reports, including PADERs, received from Hetero Labs Ltd., India to CDER, FDA. Hetero USA is also responsible for logging and determining the nature of market complaints received on behalf of Camber Pharmaceuticals, pharmaceutical distributor. According to SOP RA-03, Training Procedure, Effective Date: 11/21/2012, the head of the user department is responsible to ensure that all affected individuals are properly trained. The regulatory affairs department is also

responsible for the review and maintenance or records (**Exhibit 10**). However, the firm was unable to provide any training records pertaining to the job functions for all Hetero USA regulatory affairs personnel (**Please refer to General Discussion with Management section**).

MANUFACTURING/DESIGN OPERATIONS

POST-MARKETING ADVERSE DRUG EXPERIENCE OPERATIONS

Post-marketing adverse drug experience (PADE) activities for US marketed Hetero drug products are initiated and processed through the Pharmacovigilance and CDMA department of Hetero Labs Limited, Hyderabad, India. Periodic Adverse Drug Experience Reports (PADERs) are drafted, complied and reviewed by PV medical reviewers, drug safety associates, and senior drug safety associates located at Hetero Inc., India in accordance to their SOP PV007-00, Generation and Reporting of Periodic Adverse Drug Experience Reports (PADERs), Effective Date: April 28, 2016 (**Exhibit 11**). The reports are then forwarded to regulatory affairs personnel of Hetero USA, Piscataway for final processing and submission to the FDA. Hetero USA is also responsible for submitting annual reports for approved ANDA drug products. The PV team of Hetero Labs Ltd, India is responsible for receiving, triaging, processing and reporting individual case safety reports (ICSRs) electronically submitted through their (b) (4) System in accordance to SOP, PV001-02 Global ICSR Receipt and Date Processing, Approval Date: 01/05/2017 (**Exhibit 12**). During the inspection, we reviewed the Installment Qualification (IQ), Operation Qualification (OQ) and Performance Qualification (PQ) report, dated: 07/23/2012 for the (b) (4) software system. We also reviewed the last 15-Day Alert Report submitted to the agency in a non-electronic format: Levofloxacin, MFR No: 2015H1NLIT0803, (b) (4) Ship Date: 09/30/2015.

During the inspection, we asked Dr. Raju Indukuri, Director of Regulatory Affairs, to provide us with the quality agreements and relevant SOPs outlining the roles and responsibilities between Hetero USA, Hetero Labs Ltd, and the pharmacovigilance team. He provided us with the firm's quality agreement, dated: 12/16/2014, which outlines the regulatory submission requirements and annual reporting roles between Hetero Labs Ltd. and Hetero USA (**Exhibit 6**). He also provided us with SOP RA-01, Operations – US Regulatory Office, Effective Date: 06/06/2011, which states that Hetero USA is the US regulatory office for Hetero group, India and is responsible for ANDA submissions, amendments, annual reports and any other submissions to the FDA (**Exhibit 13**). However, the firm was unable to provide an established agreement for pharmacovigilance roles between both parties. The firm began drafting the document during the inspection and provided the approved copy of the Pharmacovigilance Agreement, Dated: 03/10/2017 (**Exhibit 14**). The agreement states that periodic report submissions and follow up reporting to safety related queries from regulatory US authorities will be the responsibility of Hetero USA, Piscataway, NJ. Dr. Ragu Indukuri confirmed that Hetero USA began submitting PADERs to the FDA since the firm's establishment in 2011. However, no standard operating procedure has been established for receiving, processing, and submitting PADERs from Hetero USA to the US regulatory agency (**Please refer to Form FDA-483 Observation 2**).

During the inspection, we confirmed that the firm continues to mail PADER submission via United Parcel Service ((b) (4) (**Please refer to Form FDA-483 Observation 3**). Dr. Raju Indukuri, Director of Regulatory Affairs, attributed the non-compliant practice due to the SRP tool for electronic submission of PADERs not being available in the (b) (4) database system currently stationed at Hetero Labs, India for ICSR submissions. He confirmed that the PV team of Hetero Labs are expected to start submitting electronic PADER submissions from May 2017 onwards. In the interim, Hetero USA will begin using their current (b) (4) system to submit PADERs in an electronic format. On 03/15/2017, the firm revised the agreement to update Hetero USA new PADER submission process through the firm's electronic system (**Exhibit 15, Page 4**). During the inspection we reviewed the (b) (4) server Installment Qualification (IQ) report, Approved: September 2010 and SPL and eCTD Operational Qualification report, Approved: November 2010. However, Dr. Raju Indukuri, Director of Regulatory Affairs confirmed that the performance qualification was not performed by the vendor. The (b) (4) software system has been used by the firm to submit annual reports to the FDA since August 2013 (**Please refer to General Discussion with Management section**).

WAIVERS

Dr. Raju Indukuri, Director of Regulatory Affairs stated that Hetero USA, Piscataway, NJ and its parent company, Hetero Inc. Hyderabad, India does not have any waivers for any of its drug products.

PATIENT ASSISTANCE PROGRAM (PAP)

Dr. Raju Indukuri, Director of Regulatory Affairs stated that Hetero USA, Piscataway, NJ and its parent company, Hetero Inc. Hyderabad, India, does not have any patient assistant programs at this time.

LITERATURE REVIEW

Literature searches are performed by the pharmacovigilance department of Hetero Labs Ltd, India, as per SOP PV004-01, Global Literature Monitoring for Hetero Products, Effective Date: May 23, 2016. Hetero products are registered with (b) (4). Hetero receives email alerts on (b) (4) basis from the search engine with abstracts concerning associated products. Literature cases are considered invalid if:

- The case does not contain an identifiable reporter, identifiable patient, drug (s) and AE(s).
- The author does not attribute any causal relationship to Hetero's suspected product
- Non company product brand names or other marketing authorization holder (MAH) is mentioned very clearly
- Duplicate literature search articles

PADERs

During the inspection, we were provided with a list of all PADERs submitted to the agency since January 2014 (**Exhibit 16**). We also asked the firm to specify each late PADER submission, the reason for late submission, and any CAPA associated with the cases. CAPAs were provided for the following cases:

- Simvastatin Tablets USP 5 mg, 10 mg, 20 mg, 40 mg, and 80 mg, ANDA Approval Date: 11/25/2014, Review Period: 02/24/2015 to 05/24/2015, Quarter 2, FDA Submission Date: 06/29/2015, Days Late: 5
- Sildenafil Citrate Tablets, 20 mg, ANDA Approval Date: 11/26/2014, Review Period: 02/25/2015 to 05/25/2015, Quarter 2, FDA Submission Date: 06/29/2015, Days Late: 4
- Lamivudine Tablets 100 mg, ANDA Approval Date: 01/02/2014, Review Period: 03/29/2015 to 06/26/2015, Quarter 6, FDA Submission Date: 07/27/2015, Days Late: 1
- Montelukast Sodium Tablets, 10 mg, ANDA Approval Date 09/10/2014, Review Period: 08/31/2016 to 11/28/2016, Quarter 9, FDA Submission Date: 12/30/2016

The firm attributed all the late submissions of the quarterly PADERs due to delay in internal approval process of reports. The reviewers were apprised of the delay and need to maintain regulatory timelines for each of the repeated instances (**Exhibit 17**). No further explanation was provided. Furthermore, we noted discrepancies in the date used to determine FDA submission date versus the (b) (4) shipment label date for submitted PADERs (**Please refer to Form FDA-483 Observation 1**).

While reviewing the list of PADER submission from January 2014 – Present, we also noted several PADERs that were not submitted during the 1st and 2nd quarter subsequent to drug product approval dates (**Please refer to Form FDA-483 Observation 1)**.

15-DAY LATE CASES

The Pharmacovigilance (PV) department of Hetero Labs Ltd, India is responsible for compiling, reviewing, and electronically submitting 15-day alert reports through their (b) (4) System in accordance to SOP PV001-02 Global ICSR Receipt and Date Processing, Approval Date: 01/05/2017 (**Exhibit 12**). Specifically, the PV team is composed of drug safety associates responsible for compiling, reporting and submitting ICSRs, senior drug safety associates responsible for reviewing the compilation of ICSRs, and medical reviewers responsible for the medical review of ICSRs. During inspectional review, Dr. Ragu Indukuri provided January 2015 – Present line listing reports of serious labeled and unlabeled cases, death cases, non-serious unlabeled cases, literature cases, and a list of late 15-day alert reports submitted to the agency (**Exhibit 18**).

During the inspection, the firm also provided us with CAPA reports for the following 15-day late cases (**Exhibit 19**):

Case ID	Reason for late submission to FDA	Source and Assessment	Drug Product	Days Late
2016HINLIT0640	Case was processed late on Day 9 (Oct 05, 2016), Medical Review was completed on Day 14 (October 10, 2016) and delayed on Day 17 (October 13, 2016)	Literature; Non-US Origin	Lithium	2
2016HINLIT0641	Case was processed late on Day 9 (Oct 05, 2016), Medical Review was completed on Day 14 (October 10, 2016) and delayed on Day 17 (October 13, 2016)	Literature; Non-US Origin	Lithium	2
2016HINLIT0642	Case was processed late on Day 9 (Oct 05, 2016), Medical Review was completed on Day 14 (October 10, 2016) and delayed on Day 17 (October 13, 2016)	Literature; Non-US Origin	Lithium	2
2016HINLIT0791	Case was processed late on Day 7 (December 19, 2016), Medical Review was completed on Day 11 (December 23, 2016) and further delay in reporting to Day 21 (Jan 02, 2017)	Literature; US Origin	Lamivudine	6
2017HINSPO0020	Case was processed late and routed to Data Review on Day 10 (January 16, 2017), Medical Review was completed on Day 15 (January 21, 2017) and reported on day 17 (Jan 23, 2017)	Literature; Non-US Origin	Levetiracetam	2
2016H1NLIT0517	The case was due for reporting on August 16, 2016, but was submitted late on August 23, 2016 due to manual reporting error.	Literature; US Origin	Lithium	7

The PV team of Hetero Labs Ltd., India did not provide any further root cause explanation for the late submissions of ICSRs. Furthermore, CAPAs were not provided for the remaining twenty five (25) 15-day late cases submitted to the agency since January 2015. For example, a serious and spontaneous case of Aplastic anemia involving Linezolid, 600mg was received by Hetero Labs Ltd., Hyderabad India on 11/19/2015 via the (b) (4) (b) (4)). However, the 15-day report was not submitted to the FDA until December 6, 2016, 367 days later **(Exhibit 20**). No further explanation or CAPA was provided by the parent company for the late submission.

ANNUAL REPORTS

Hetero USA, Piscataway NJ is responsible for submitting regulatory annual reports to the agency for approved ANDA drug products. During the inspection, we requested and reviewed the list of annual reports submitted from January 2014 – Present (**Exhibit 21**). During the inspection, Mr. Rajesh Kankula, Manager of Regulatory Affairs, walked us through the submission process of annual reports using the firm's (b) (4) software system; the 2017 annual report for Levofloxacin Tablets, 250 mg, 500 mg and 750 mg was used as an example. We confirmed the submission file contained all the necessary requirements for annual reporting, including the FDA Form 2252, summary of clinical and non-clinical studies, summary of safety information, and summary of labeling and manufacturing changes. We also reviewed the submission receipt received from FDA electronic submissions gateway (ESG), Dated: 03/06/2017 for the same drug product. No deficiencies were noted.

OVERSIGHT/AUDITS

During the inspection, I asked Dr. Raju Indukuri, Director of Regulatory Affairs if there were any periodic meetings or reconciliation performed between Hetero Labs Ltd, India, Camber Pharmaceuticals and Hetero USA regarding PADER submissions, annual reporting, and the complaint handling process for various US marketed products. Mr. Indukuri stated that he occasionally visits and holds meetings with the Hetero Labs Limited, India Quality Assurance and PV department. However, he was unable to provide any documents or meeting minutes for complaint reconciliation, PV audits and/or PADER reviews performed between Hetero USA, Camber Pharmaceuticals and Hetero, the parent company (**Please refer to General Discussion with Management section**).

COMPLAINTS

During the inspection, we reviewed various January 2015 – February 2017 product quality complaints and ADR reports that have been received by Hetero USA, Piscataway, NJ on behalf of Chamber Pharmaceuticals Inc., the pharmaceutical distributor. During the inspection, we noted that Hetero USA has not developed a standard operating procedure for logging, processing and handling complaints received from Camber Pharmaceuticals' customer service department and for forwarding the complaints to Hetero Labs Ltd., India for further triage, investigation and final reporting (**Please refer to Form FDA-482 Observation 2**). We also noted deficiencies in the firm's complaint handling and documentation practice (**Please refer to General Discussion with Management section**).

DRUG QUALITY SYSTEM REPORTS (DQRS)

During the inspection, we reviewed the firm's complaint and investigation logs against DQRS reports processed through FDA CDER, Office of Pharmaceutical Quality, Quality Deviation Assessment Brand (QDAB). Entry receipt logs and investigation reports were reviewed for the following drug product complaints:

FDA MSB #	Notification Date	Hetero USA Complaint #	Product Information	Product Complaint Description
2017-02062	01/23/2017	2017 Year Quarter I, Serial No. 11	Pantoprazole Sodium, 40 mg, 90 count bottle, Lot #PAN16253, Exp. Date: Unknown	Reflux system when started new batch
2016-02598	02/17/2016	2016 Year, Quarter I, Serial No. 58	Pantoprazole Sodium, 40 mg, 90 count bottle, Lot #PAN215007; Exp. Date: 05/31/17	Lack of therapeutic effect
2016-01075	12/09/2015	2015 Quarter IV, Serial No. 81	Valsartan, 80 mg, 90 count bottle, lot #VLS214003, Exp. Date: 11/30/16	Anxiety and irritability after switching brands
2016-03489	03/19/2016	2016 Year Quarter I, Serial No. 112	Irbesartan, 150 mg, 90 count bottle, lot # IST215021, Exp. Date: Unknown	Acute hypertensive crisis following 2nd dose of drug product
2016-05066	05/23/2016	2016 Year, Quarter II, Serial No. 25	Montelukast Sodium, 10 mg, 90 count bottle, lot # 50/MN/AP/2009/F, Exp Date: Unknown	Severe headaches, dizziness, fatigue, and hazy feelings
2016-05741	06/24/2016	2016 Year, Quarter II, Serial No. 44	Esomeprazole Magnesisum, 40 mg, 1000 count bottle, lot # E151866, Exp. Date: 04/30/17	Med not working and all symptoms of gastroesophageal reflux disease are back

During our review, we noted deficiencies in the firm's complaint handling practices and in logging batch information contained in DQRS reports (**Please refer to General Discussion with Management section**).

FIELD ALERT REPORTS (FAR)

According to Dr. Ragu Indukuri, Director of Regulatory Affairs, Hetero USA is responsible for handling complaints, field alert report submissions, and recall activities for generic drug products marketed in the United States under the Camber Pharmaceuticals Inc. brand name. Hetero Corporate, Hyderbad, India is also responsible for carrying out product investigations, compiling field alert reports and forwarding the report to Hetero USA, Piscataway, NJ for final submission to the FDA. During the inspection, coverage for the submission of field alert reports was provided for the following marketed drug products:

FAR Due Date	Initial Submission Date	FAR Follow-up submission dates	Drug Product Information	Complaint Reasoning
01/13/2013	01/10/2013	First follow-up: 01/25/2013 Final follow -up: 02/25/2013	Lithium carbonate capsules, Batch No: E121247	Complaint: Bottle containing capsules stuck together and some powder was out of capsule
07/13/2016	07/11/2016	Final follow-up: 08/10/2016	Finasteride tablets USP 5mg, FIN16002	Complaint: The filling of a prescription for Finasteride 5 mg and noticed one tablet in bottle was twice the thickness of all the others and it had the same markings and color as the other tablets
07/11/2016	07/15/2016	First follow-up: 08/04/2016 Final follow-up: 11/19/2016	Montelukast sodium tablets 10 mg, lot # MON16001B	Complaint: received a sealed bottle of Montelukast in which all the tablets and the inside of the bottle were coated in blue powder
02/18/2017	02/18/2017	First follow-up: 03/09/2017	Acyclovir tablets, USP 800 mg, lot # ACY16075	Complaint: During repacking production run, discovered what appears to be a human hair molded into tablet

We reviewed a total of four (4) Field Alert Reports (FARs) submitted to the FDA since the previous inspection. During our review, we noted that the firm received a complaint pertaining to Montelukast sodium tablets 10 mg, lot # MON16001B on July 07, 2016. However the firm did not file a field alert with the agency until July 15th, 2016, which is four (4) days later than the FAR due date (**Please refer to General Discussion with Management section**).

OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE

Observations listed on form FDA 483

OBSERVATION 1

Not all quarterly periodic adverse drug experience reports have been submitted within 30 days of the close of the quarter.

Specifically,

The firm has failed to submit approximately ten (10) periodic adverse drug experience reports (PADERs) between January 2014 and February 2017 for various US marketed finished drug products, including:

Drug Product	ANDA Number	ANDA Approval Date	Missing PADER Quarter	Missing PADER Review Period	Submission Status
Famciclovir Tablets, 125 mg, 250 mg, and 500 mg	202438	09/10/2014	Q1	09/10/2014 to 12/09/2014	No Submission
Famciclovir Tablets, 125 mg, 250 mg, and 500 mg	202438	09/10/2014	Q2	12/10/2014 to 03/09/2015	No Submission
Pantoprazole Sodium Delayed-release Tablets USP, 20 mg and 40 mg	202882	09/10/2014	Q1	09/10/2014 to 12/09/2014	No Submission
Pantoprazole Sodium Delayed-release Tablets USP, 20 mg and 40 mg	202882	09/10/2014	Q2	12/10/2014 to 03/09/2015	No Submission
Montelukast Sodium Tablets, 10 mg	202843	09/10/2014	Q1	09/10/2014 to 12/09/2014	No Submission
Montelukast Sodium Tablets, 10 mg	202843	09/10/2014	Q2	12/10/2014 to 03/09/2015	No Submission

Sildenafil Citrate Tablets, 20 mg	203623	11/26/2014	Q1	11/26/2014 to 02/24/2015	No Submission
Lamivudine and Zidovudine Tablets 150 mg/300 mg	203259	02/03/2014	Q1	02/03/2014 to 05/04/2014	No Submission
Simvastatin Tablets USP, 5 mg, 10 mg, 20 mg, 40 mg and 80 mg	200895	11/25/2014	Q1	11/25/2014 to 02/23/2015	No Submission
Levofloxacin Tablets USP, 250 mg, 500 mg, and 750 mg	202801	01/08/2015	Q1	01/08/2015 to 04/08/2015	No Submission

In addition, the following PADERs were not submitted in a timely manner:

Drug Product	**ANDA Number**	**ANDA Approval Date**	**PADER Quarter**	**PADER Review Period**	**FDA Submission Date**	**Days Late**
Simvastatin Tablets USP, 5 mg, 10 mg, 20 mg, 40 mg and 80 mg	200895	11/25/2014	Q2	02/24/2015 to 05/24/2015	06/29/2015	5
Sildenafil Citrate Tablets, 20 mg	203623	11/26/2014	Q2	02/25/2015 to 05/25/2015	06/29/2015	4
Lamivudine Tablets 100 mg	203260	01/02/2014	Q6	03/29/2015 to 06/26/2015	07/27/2015	1
Montelukast Sodium Tablets, 10 mg	202843	09/10/2014	Q9	08/31/2016 to 11/28/2016	12/30/2016	2

Reference: 21 CFR 314.80(c)(2)

Supporting Evidence and Relevance:
Exhibit # 16, 17, 22 - 33

Discussion with Management:

On March 8th, 2017, the firm provided a line listing of periodic adverse drug event reports (PADERs) submitted to the agency from January 2014 to Present (**Exhibit 22**). While reviewing the line listing report, we noted that there were several missing quarterly and annual PADER submissions for approved ANDA drug products. When we pointed this out to the firm, Mr. Soma Ragu Indukuri, Director of Regulatory Affairs, stated that he was unsure as why the line listing report did not contain the missing quarterly and annual PADER submissions and would contact the pharmacovigilance team of Hetero, India to gain further explanation. He further stated that the line listing report might also be deficient in listing all the up to date information. We asked him to reconcile any missing submissions and provide a copy of the dated PADER submission letter, shipment label, and FDA receipt letter for each submission not reflected in the line listing report. On March 9, 2017, Mr. Indukuri, Director of Regulatory Affairs, reconciled and provided PADER submission letters, shipment labels and receipt letters for several of the unlisted PADER submissions. The firm then provided us with a list of the remaining ten (10) first quarter and/or second quarter PADERs that were not submitted to the agency (**Exhibit 23**). Mr. Indukuri, Director of Regulatory Affairs, also provided us with a copy of the deviation report initiated on 03/13/2017 by Hetero Labs Ltd. pharmacovigilance department for the missing PADER submissions (**Exhibit 24**). According to the unplanned deviation report, five (5) out of the ten (10) missing PADERS had no reported cases and the remaining five missing PADERs had cases that were not eligible for PADER inclusion. I then requested and reviewed the completed MedWatch 3500A forms, CIOMS forms and/or investigation reports associated with the missing PADERs for the following drug products:

- Levofloxacin Tablets USP, 250 mg, 500 mg, and 750 mg, ANDA Approval Date: 01/08/2015 (**Exhibit 25**)
- Simvastatin Tablets USP, 5 mg, 10 mg, 20 mg, 40 mg and 80 mg, ANDA Approval Date: 11/25/2014 (**Exhibit 26**)
- Sildenafil Citrate Tablets, 20 mg, ANDA Approval Date: 11/26/2014 (**Exhibit 27**)
- Montelukast Sodium Tablets, 10 mg, Approval Date: 09/10/2014 (**Exhibit 28**).

During my review, I noted that there were various ADE cases submitted as 15-Day Alert reports that the firm has disqualified for PADER inclusion and reporting for the missing submission time periods. The ADE cases were received by the firm subsequent to ANDA approval date of the Hetero drug product. Below are some of the US reported cases associated with the missing PADER submission time periods:

Drug Product; FDA Approval Date	**ANDA Approval Date**	**MedWatch 3500A MFR Report/ Control #**	**Country of Incident; Date Received**	**ADE Description**	**ADE Case Assessment & Report Type**

Levofloxacin Tablets USP, 500 mg	01/08/2015	2015HINLIT0088 – Literature Case (**Exhibit 25, Page 10**)	Arizona, US; Received On: 01/27/2015	E. coli infection, epidymo-orchitis, bacteraemia, bacteriuria, and meningitis	Serious and unlisted; Initial 15 day report
Levofloxacin; Non-specified Dose and Route	01/08/2015	2015HINLIT0088 – Literature Case (**Exhibit 25, Page 22**)	United States; Received On: 02/24/2015	Drug induced Cholestasis and Cholangitis	Serous and unlisted; 15 day report
Levofloxacin; Non-specified Dose and Route	01/08/2015	2015HINLIT0222 – Literature Case (**Exhibit 25, Page 26**)	United States; Received On: 02/24/2015	Hepatotobiliary toxicity, hepatic failure and Stevens-Johnson syndrome	Serious and unlisted; 15 day report
Simvastatin; Non specified and Route	11/26/2014	2015HINLIT0063 – Literature Case (**Exhibit 26, Page 26**)	United States; Received on 01/20/2015	Nausea and Vomiting	Serious and suspected; 15 day report
Simvastatin; Non specified and Route	11/26/2014	2015HINLIT0110 – Literature Case (**Exhibit 26, Page 29**)	United States: Received on 01/27/2015	Lipid storage myopathy	Serious and unlisted; 15 day report

When I pointed this out to Dr. Ragu Indukuri, Director of Regulatory Affairs, he stated that he was unsure of the discrepancies between the evaluation performed and the conclusion stated in Hetero Lab's deviation report versus the MedWatch 3500A/CIOMS forms for US reported cases received subsequent to drug product approval dates.

On 03/16/2017, the firm provided an updated list of PADERs submitted between January 2014 and March 2017 (**Exhibit 16**). During my review, I noted that the firm classifies their FDA submission date as the date listed on the PADER submission letter. However, there were several instances in which Hetero USA did not process and submit the PADERs to the agency until days later. For example:

- The PADER line listing report states that Lamivudine Tablets, 100 mg, Quarter 5, Review Period: 12/29/2014 to 03/28/2015 was submitted on 04/23/2015 (**Exhibit 16, Page 9**). However, the shipment label from Hetero USA, Piscataway, NJ to Office of Generic Drugs (OGD), CDER, FDA was dated 04/28/2015 (**Exhibit 29, Page 2**)

- The PADER line listing report states that Simvastatin Tablets USP, 5mg, 10 mg, 20 mg,40 mg and 80 mg, Quarter 2, Review Period: 02/24/2015 to 05/24/2015 was submitted on 06/25/2015 (**Exhibit 16, Page 14**). However the shipment from Hetero USA to OGD, CDER FDA was dated 06/29/2015 (**Exhibit 30, Page 2**).

Lastly, CSO Bernard and I noted various instances in which quarterly PADERs were submitted after 30 days of the close of the quarter. We then requested and reviewed PADER reports, submission letters, shipment labels, and FDA receipt letters for the following late PADER submissions:

Drug Product	ANDA Number	ANDA Approval Date	PADER Quarter	PADER Review Period	FDA Submission Date	Days Late
Simvastatin Tablets USP, 5 mg, 10 mg, 20 mg, 40 mg and 80 mg	200895	11/25/2014	Q2	02/24/2015 to 05/24/2015	06/29/2015 (**Exhibit 30, Page 2**)	5
Sildenafil Citrate Tablets, 20 mg	203623	11/26/2014	Q2	02/25/2015 to 05/25/2015	06/29/2015 (**Exhibit 31, Page 2**)	4
Lamivudine Tablets 100 mg	203260	01/02/2014	Q6	03/29/2015 to 06/26/2015	07/27/2015 **(Exhibit 32, Page 2**)	1
Montelukast Sodium Tablets, 10 mg	202843	09/10/2014	Q9	08/31/2016 to 11/28/2016	12/30/2016 (**Exhibit 33, Page 2**)	2

Dr. Indukuri, Director of Regulatory Affairs, attributed the late PADER submissions due to delay in processing by the pharmacovigilance department. He also provided the corrective and preventative action reports for each of the late submissions, which still did not reflect the actual dates in which Hetero USA submitted the PADERs to OGD, CDER FDA (**Exhibit 17**). Dr. Indukuri acknowledged the discrepancy and stated that future PADERs will be documented to reflect actual submission dates to the FDA. During the closeout meeting, I reiterated my concerns to management and emphasized the importance of submitting quarterly and annual PADERs in a timely manner. Dr. Indukuri stated that the firm would take corrective actions by implementing standard operating procedures to better ensure that PADERs are appropriately processed and submitted to the FDA in a timely fashion.

OBSERVATION 2
Written procedures have not been developed for the receipt and reporting to FDA of post marketing adverse drug experiences.

Specifically,

Hetero USA is responsible for receiving US postmarketing periodic safety reports (PADERs) compiled by the firm's parent company and submitting the compiled PADERs to the FDA. However, no written procedure has been established for the receipt and submission of PADERs by Hetero USA.

In addition, Hetero USA is responsible for handling customer complaints and product recalls as per established agreement between Hetero USA and the pharmaceutical distributor for US marketed drug products. However, the firm has not developed a written procedure for receiving, logging, and forwarding customer complaints, which includes reported adverse drug events, to the drug product manufacturer for further assessment.

Reference: 21 CFR 314.80(b)

Supporting Evidence and Relevance:
Exhibit #7, 11, 13, 14, 34 - 39

Discussion with Management:
Hetero USA, Piscataway, NJ is the regulatory agent of Hetero Labs Ltd, India and is responsible for submission of ANDAs, amendments, supplements, annual reports, the receipt of FDA correspondence, and follow-up with FDA and post approval activities for generic finished dosages (**Exhibit 13, Page 1**). Hetero USA is also responsible for the mailing, submitting, and receiving FDA receipt of acknowledgements for periodic reports sent to the regulatory authority (**Exhibit 14, Page 4 and 5**). Hetero Labs Ltd. is responsible for preparing and generating PADERs and forwarding the complete report to Hetero USA for final submission to the FDA. During the inspection, Mr. Indukuri, Director of Regulatory Affairs, provided us with copies of firm's SOP index (**Exhibit 34**) and standard operating procedures for the regulatory affairs department. We noted that there were no SOPs pertaining to the receipt and submission of PADERs. I also pointed that that the procedure established by and for the PV department of Hetero Corporate, India does not mention the mailing, submission, and acknowledge receipt process for regulatory affairs personnel at Hetero USA (**Exhibit 11**). Therefore, there should be an SOP pertaining to Hetero USA's independent PADER receipt and submission process. Mr. Indukuri, Director of Regulatory Affairs, acknowledged the oversight and stated that the firm will update their standard operating procedures accordingly to include their handling and submission process for periodic reports.

Furthermore, Hetero USA Inc. is also responsible for handling customer complaints, product recalls, training, and scientific and regulatory affairs activities on behalf of Camber Pharmaceuticals, Inc., the pharmaceutical distributor for Hetero Labs Ltd., India (**Exhibit 7**). However, Hetero USA has not developed a standard operating procedure for logging, processing and handling complaints received from Camber Pharmaceuticals Inc. customer service department and forwarding the complaints to Hetero Labs Ltd., India for further triage, investigation and final reporting. Dr. Ragu Indukuri, Director of Regulatory Affairs, provided an uncontrolled sheet of paper that lists the steps

that the customer service department takes to forward complaints that are then logged and processed by Hetero USA regulatory affairs personnel for further investigation (**Exhibit 35**). He also provided Camber Pharmaceuticals' procedure, SOP 23, Market Complaints, Effective Date: 01/12/2017, for handling incoming customer complaints received by the pharmaceutical distributor (**Exhibit 36**). Mr. Indukuri stated that market complaints are forwarded by Camber Pharmaceutical customer service representatives to Mr. Raghunath Chigurpati, Manager of Regulatory Affairs, who then logs, evaluates and forwards the complaints for further investigation by the manufacturer. Mr. Chigurupati explained that part of his responsibilities is determining which complaints are product quality complaints versus adverse drug reactions (ADR) and then forwards the complaint to either the manufacturing and/or Pharmacovigilance department of Hetero Labs Ltd. For example, a consumer complaint report was received by the firm on 1/02/2016 due to foul taste being experienced for Finasteride Tablets USP, 5 mg. The complaint was initially received from (b) (4) (b) (4), a pharmaceutical distributor, then logged by Mr. Chigurpati, Manager of Regulatory Affairs, as a quality related complaint and forwarded to the manufacturing department of Hetero Labs Ltd. Unit III for further investigation (**Exhibit 37, Page 1**). I reviewed the complete investigation, which states that the complaint investigation report was eventually forwarded to the Pharmacovigilance team by Hetero Labs Ltd QA department for further investigation (**Exhibit 38, Page 13**). A MedWatch 3500A 15-day alert report was also generated for the consumer complaint (**Exhibit 38, Page 14**). Lastly, Dr. Indukuri and Mr. Chigurpati were unable to provide any training records in regards to logging, processing, evaluating, and forwarding product quality and ADRs for further investigation. The firm was also unable to provide documentation of complaint reconciliations or auditing performed between Hetero USA, Chamber Pharmaceuticals and Hetero Labs Ltd. During the inspectional closeout meeting, I reiterated my concerns for the firm's lack of standard operating procedure for logging, evaluating, and forwarding complaints to their drug product manufacturer for further investigation. Dr. Indukuri understood my concerns and stated the firm plans to (b) (4) ., (b) (4) (**Exhibit 39**).

OBSERVATION 3
You did not submit adverse drug experience information in electronic format.

Specifically,

Your firm has failed to submit postmarketing periodic safety reports (PADERs) reported since September 8, 2015 in an electronic format. For example:

- The quarterly PADER for ANDA# 203623 Sildenafil Citrate Tablets, 20 mg, review period: 11/16/2016 to 02/13/2017, was submitted by the firm on March 06, 2017 via courier delivery service.

- The quarterly PADER for ANDA# 205740 Entecavir Tablets, 0.5 mg, review period: 11/14/2016 to 02/11/2017, was submitted by the firm on March 02, 2017 via courier delivery service.

- The quarterly PADER for ANDA# 202843 Montelukast Sodium Tablets, 10 mg, review period: 08/31/2016 to 11/28/2016, was submitted by the firm on December 30, 2016 via courier delivery service.

Reference: 21 CFR 314.80(c)

Supporting Evidence and Relevance:
Exhibit # 15, 40 - 43

Discussion with Management:
During the inspection, CSO Bernard and I confirmed that the firm continues to submit PADERs from Hetero USA, Piscataway, NJ to OGD, CDER, FDA via courier delivery services. For example:

- The quarterly PADER for ANDA# 203623 Sildenafil Citrate Tablets, 20 mg, review period: 11/16/2016 to 02/13/2017, was manually submitted by Hetero USA on March 06, 2017 through (b) (4) (**Exhibit 40**).
- The quarterly PADER for ANDA# 205740 Entecavir Tablets, 0.5 mg, review period: 11/14/2016 to 02/11/2017, was manually submitted by Hetero USA on March 02, 2017 through (b) (4) (**Exhibit 41**).
- The quarterly PADER for ANDA# 202843 Montelukast Sodium Tablets, 10 mg, review period: 08/31/2016 to 11/28/2016, was manually submitted by Hetero USA on December 30, 2016 through (b) (4) (**Exhibit 33).**

During the inspection, Dr. Ragu Indukuri, Director of Regulatory Affairs, also provided step-by-step instructions for receiving, processing and submitting completed PADERS to the agency (**Exhibit 42**). This set of instructions states to print out the PADERs, generate (b) (4) shipping labels, and forward the package to the FDA along with a copy of the return receipt placed in a Hetero USA envelope. Dr. Ragu Indukuri also confirmed that he received the FDA Compliance letter, Dated: 10/06/2015 for electronic submission requirements for all postmarketing drug safety reports subsequent to September 8, 2015 (**Exhibit 43**). Dr. Ragu Indukuri stated he mistakenly thought the electronic submission requirements were only applicable to ICSRs, hence why the reason why PADERs are not submitted in electronic format. He further attributed the non-compliant practice due to the SRP tool for electronic submission of PADERs not being available in the (b) (4) database system currently stationed at Hetero Labs, India for ICSR submissions. I explained that the final rule for Postmarketing Safety Reports for Human Drug and Biological Products: Electronic Submission Requirements applies to all postmarketing drug safety reports in accordance to 21 CFR 314.80 and as outlined in the compliance letter. Dr. Ragu Indukuri acknowledged the oversight and stated that the firm would immediately implement electronic submission of PADERs through their (b) (4) system, which is currently used to submit annual reports. On 03/15/2017, the firm also revised their quality agreement to update Hetero USA new PADER submission process through the firm's electronic system (**Exhibit 15, Page 4**). During the closeout meeting, Dr. Ragu

Indukuri, Director of Regulatory Affairs and Mr. Akula, Executive Vice President understood my concerns and promised to ensure that all future PADERs are submitted in an electronic format.

GENERAL DISCUSSION WITH MANAGEMENT

On 03/17/2017, an inspectional closeout meeting was held with the firm's management and a Form FDA-483, Inspectional Observations, was issued to Mr. Seshu Akula, Executive Vice President. Also present were Dr. Soma Ragu Indukuri, Director of Regulatory Affairs, Mr. Raghunath Chigurupati, Manager of Regulatory Affairs, and Mr. Rajesh Kankula Manager of Regulatory Affairs. The following deficiencies were also verbally discussed with the firm's management team:

Deficiencies in Complaint Handling

During the inspection, we reviewed complaint logs for all adverse drug reactions (ADRs) and product quality related complaints received from January 2015 – Present. We also reviewed the complaint handling process, investigations reports, and applicable MedWatch 3500A forms for various logged complaints. During our review of the complaint against Drug Quality System Reports (DQRS) received by the firm, we noted deficiencies in good documentation practices. For example:

- The firm received a DQRS report for Esomeprazole Magnesium, 40 mg, Lot # E151886, Exp. Date: 04/30/2017 from the agency on 06/24/2016 on behalf of Camber Pharmaceuticals, Piscataway, NJ (**Exhibit 44**). However, the market complaint logbook listed the drug product batch number and expiration date as "N/A" (**Exhibit 45, Page 8**).

- In another instance, the firm received a DQRS report for Irbesartan 150 mg, Lot # IST215021, Exp. Date: Not Given, on 03/19/2016 on behalf of Camber Pharmaceuticals (**Exhibit 46**). However, the market complaint logbook listed the drug product batch number as "N/A" (**Exhibit 47, Page 12**).

- Lastly, the firm received a DQRS report for Valsartan, 80 mg, Lot# VLS124003, Exp. Date: 11/30/2016 on 12/09/2015 on behalf of Camber Pharmaceuticals (**Exhibit 48**). However, the market complaint logbooks listed the drug product batch number and expiration date as "N/A" (**Exhibit 49, Page 9**).

When I pointed this out to Mr. Raghunath Chigurpati, Manager of Regulatory Affairs, he stated that the complete complaint information was not logged due to DQRS letters being already forwarded to Hetero Labs Limited, India for investigational purposes. I then requested and reviewed the completed MedWatch 3500A forms for Esomeprazole Magnesium, 40 mg, Lot # E151886, Exp. Date: 04/30/2017, Irbesartan 150 mg, Lot # IST215021, and Valsartan, Lot# VLS124003, Exp. Date: 11/30/2016. I confirmed that the MedWatch 3500A reports contained the complete lot number and/or expiration dates that were not reflected in the market complaint logbook. I also noted that the

complaint logbooks are sometimes reviewed, signed and dated by the same personnel logging the complaints. For example, Mr. Chigurpati, Manager of Regulatory Affairs, confirmed that he logged 2016 Quarter IV complaints received from 10/03/2016 to 12/28/2016. However, he also confirmed that he signed off the complaint logbook for review on 01/05/2017 (**Exhibit 50**). Mr. Chigurpati, Manager of Regulatory Affairs, stated that Dr. Ragu Indukuri, Director of Regulatory Affairs, is normally responsible for reviewing and signing off complaint logbooks. However, Dr. Ragu Indukuri instructs him to sign off the complaint logbook whenever he is too busy to complete the task. Lastly, the firm was unable to provide any documentation of complaint reconciliation or auditing performed between Hetero USA, Hetero Labs Ltd., and/or Camber Pharmaceuticals. During the inspectional closeout meeting, I explained to the firm's management team the importance of adhering to good documentation when logging adverse drug experiences (ADEs) and product complaints received on behalf of Chamber Pharmaceuticals, the pharmaceutical distributor. Dr. Ragu Indukuri and Mr. Seshu Akula, Executive Vice President, both understood my concerns and promised to ensure that all future complaints are appropriately logged and reviewed by Hetero USA. He further stated that Camber Pharmaceuticals plans to (b) (4) [redacted] (**Exhibit 39**).

Lack of Documented Oversight, Reconciliation or Audits performed between Hetero USA, Camber Pharmaceuticals Inc. and Hetero Labs Ltd, India

During the inspection, I asked Dr. Raju Indukuri, Director of Regulatory Affairs if there were any periodic meetings or reconciliation performed between Hetero Labs Ltd, India, Camber Pharmaceuticals and Hetero USA for PADER submissions, annual reporting, and complaint handling of various US marketed products. Mr. Indukuri stated that he occasionally visits and holds meetings with the Hetero Labs Limited Quality Assurance and the PV department located in Hyderabad, India. However, he was unable to provide any documents or meeting minutes for complaint reconciliation, PV audits and/or PADER reviews performed between Hetero USA, Camber Pharmaceuticals and Hetero Corporate, India. During the inspectional closeout meeting, I reiterated my concerns for ensuring oversight of all pharmacovigilance and PADE activities between Hetero USA and its partners are documented and performed.

Lack of Training Records

Hetero USA is responsible for receiving, mailing and submitting periodic reports, including PADERs, received from Hetero Labs Ltd., India to CDER, FDA. Hetero Lab Ltd is responsible for preparing and generating PADERs and relaying the final copy for submission to the FDA. Hetero USA is also responsible for logging and determining the nature of market complaints received on behalf of Camber Pharmaceuticals, pharmaceutical distributor. However, the firm was unable to provide any training records pertaining to personnel responsibilities in PADER receipt and submission, annual reporting, and complaint handling processes. Dr. Ragu Indukuri provided job descriptions and resumes for each of the regulatory personnel involved in such processes, including:

Mr. Raghunath Chigurupati, Manager of Regulatory Affairs (**Exhibit 51**)

Mr. Rajesh Kankula, Manager of Regulatory Affairs (**Exhibit 52**).

Dr. Soma Raju Indukuri, Director of Regulatory Affairs (**Exhibit 53**).

During the inspectional closeout meeting, I reiterated the importance of ensuring all personnel involved in post marketing activities for approved drug products are appropriately trained in accordance to their job function. Mr. Akula, Executive Vice President understood my concerns and stated that re-training for regulatory affairs personnel will be conducted, documented, and reviewed in accordance to SOP RA-03, Training Procedure, Effective Date: 11/21/12 (**Exhibit 10**).

Lack of Performance Qualification/Testing for (b) (4) ***software***

On 03/16/2017, Dr. Ragu Indukuri provided a copy of their first PADER submitted to the agency electronically through (b) (4) software. I then requested the Installment, Operational, and Performance Qualification performed for the software system. I confirmed that the installment and operational qualification were completed in September 2010 and November 2010 respectively. When I inquired about the missing performance qualification, Mr. Ragu Indukuri, Director of Regulatory Affairs stated he was not aware a performance qualification was necessary given the completed operation qualifications. He further stated that he would contact the vendor to provide explanation as to why performance testing was not performed. The (b) (4) software system has been used by the firm to submit annual reports to the FDA since August 2013. Upon my return to the firm on 03/17/2017, Dr. Ragu Indukuri, Director of Regulatory Affairs, provide the performance qualification report for (b) (4), which was dated for completion on the same day (**Exhibit 54**). I explained to Mr. Indukuri, the importance of ensuring and qualifying end user acceptance of software systems prior to usage. During the closeout meeting, Dr. Ragu Indukuri, Director of Regulatory Affairs and Mr. Akula, Executive Vice President understood my concerns promised to evaluate their software validation requirements and ensure that all future PADERs are submitted in an electronic format.

Submission of Annual PADER in place of Quarterly PADER

On March 8th, 2017, the firm provided a line listing of periodic adverse drug event reports (PADERs) submitted to the agency from January 2014 to Present (**Exhibit 22**). While reviewing the PADER submission line listing, we noted discrepancies in the PADERs submitted for Linezolid tablets, 600 mg, Approval Date: 12/21/2015 (**Exhibit 22, Page 4**). Specifically, the report states that an annual PADER was submitted on May 02, 2016 for the review period of April 03, 2015 to April 02, 2016. Dr. Soma Raju Indukuri, Director of Regulatory Affairs, stated that the firm decided to prepare and submit an annual PADER subsequent to the tentative approval of Linezolid tablets, 600 mg in April 2015. The drug product was officially approved by the agency on December 21, 2015. The initial Annual PADER was complete and submitted on May 2, 2016. The firm began submitting PADERs on a quarterly basis on July 18, 2016 for the review period of March 21, 2016 to June 18, 2016. However, there was no quarterly PADER submitted for the review period between December

21, 2015 and March 21, 2016. I explained to Mr. Soma Raju Indukuri, Director of Regulatory Affairs, that although quarter one (1) postmarketing information was captured in the annual PADER used during the tentative approval of Linezolid tablets, 600 mg, it is important that the firm adhere to regulatory submission requirements for submitting PADERs on a quarterly basis subsequent to ANDA approval. During the inspectional closeout meeting, Dr. Raju Indukuri, Director of Regulatory Affairs, understood my concerns and promised to ensure that quarterly PADERs are submitted regardless of overlap between Annual PADERs submitted subsequent to the tentative approval of drug products.

Late Submission of Field Alert Report (FAR)

During the inspection, we reviewed all field alert reports filed by the firm since the previous 2011 inspection. During our review, we noted that the firm received a complaint on July, 07, 2016 for Montelukast sodium tablets 10 mg, lot # MON16001B concerning tablets coated with blue powder. However, the field alert was filed on July 15, 2016, which is four (4) days later than the FAR due date (**Exhibit 55**). The firm initiated the investigation for the complaint filed under MCU16-009 and completed their investigation on July 15, 2016. The investigation was initiated to determine the source of the blue powder. Dr. Ragu Indukuri, explained that the firm initially concluded that a field alert was not necessary due to the outcome of the final investigation and confirmed product quality through physical, microbial and analytical testing. However, he contacted the NWJ-DO field alert monitor on July 14, 2016 to confirm the nature of the complaint and their decision not to file a FAR. After further discussion with the NWJ-DO field alert monitor, the firm decided that a FAR was appropriate and subsequently filed the initial FAR for the drug product complaint on 07/15/2016. During the inspection, I explained to Dr. Ragu Indukuri, the importance of ensuring that initial FARs are filed in a timely manner for drug products subsequent to the discovery of non-conformance issues. A FAR is not required only if the problem can be invalidated within three working days of the problem being identified. He understood my concern and promised to file future FARs in a timely manner regardless of the drug product investigation status.

REFUSALS
No refusals were encountered.

VOLUNTARY CORRECTIONS
During the inspection, voluntary correction for one (1) Inspectional Observation from the previous inspection conducted from 07/19 – 20/2011 was verified**:**

OBSERVATION 1

An NDA-Field Alert Report was not submitted within three working days of receipt of information concerning an incident that caused a drug product or its labeling to be mistaken for another article.

Specifically, your firm became aware of a foreign tablet complaint for Torsemide Tablets 100mg, lot E100688, on or around 02/25/2011, but did not file an NDA Field Alert Report until 05/05/2011, approximately 49 working days later. The foreign tablet was concluded to have come from a previous batch manufactured on the same equipment, and resulted in a recall of the lot on 5/2011.

Voluntary Corrections:

During the current inspection, we reviewed and verified the submission of the initial and final follow-up field alert report (FAR) for Torsemide Tablets, 100 mg, lot #E10068 (100's Count, NDC #31722-532-01) by Hetero USA. We also verified that the recall of the drug product lot was performed and completed in December 2011 under Recall #D-721-2011. During the inspection, we also provided follow-up on a total of four (4) FARs submitted to the FDA since the previous inspection. During our review, we noted that the firm received a complaint pertaining to Montelukast sodium tablets 10 mg, lot # MON16001B on July 07, 2016. However the firm did not file a field alert with the agency until July 15th, 2016, which is four (4) days later than the FAR due date (**Please refer to General Discussion with Management section**).

EXHIBITS COLLECTED

1(GU) Hetero Company PowerPoint , 7 pages
2(GU) Hetero Reporting Structure , 1 page
3(GU) Hetero USA Product List , 8 pages
4(GU) List of Pending ANDAs, 2 pages
5(GU) List of Withdrawn ANDAs, 1 page
6(GU) Hetero USA and Hetero Labs Ltd Quality Agreement , 3 pages
7(GU) Hetero USA and Chamber Pharmaceuticals Agreement , 3 pages
8(GU) Hetero USA Organization Chart , 1 page
9(GU) Hetero Pharmacovigilance Chart , 1 page
10(GU) SOP RA-03, Training Procedure, Effective: 11/21/12, 1 page
11(GU) Hetero PV SOP No. PV007-00, Generation & Reporting of Periodic Adverse Drug Experience Reports (PADERs), Effective Date: 04/28/2016, 12 pages
12(GU) Hetero PV SOP PV-001-02, Global ICSR Receipt and Data Processing, Effective Date: 01/30/2017, 20 pages
13(GU) Hetero USA SOP RA-01, Operations - US Regulatory Office, Effective Date: 06/06/11, 3 pages
14(GU) Hetero Labs & Hetero USA Inc PV Agreement, Dated: 03/10/2017 , 6 pages
15(GU) Hetero Labs & Hetero USA PV Agreement, Dated: 03/15/2017 , 6 pages
16(GU) Updated PADER List Jan 2014 - March 2017 , 16 pages
17(GU) CAPA forms for Delayed PADERs , 5 pages

18(GU) List of 15-day Late Cases, 1 page
19(GU) CAPA Forms 15-Day Late Cases, 3 pages
20(GU) 15-Day Late Case for Linezolid Tablets, Logbook #2016/051, S. No-3, 11 pages
21(GU) List of Annual Report Submissions , 5 pages
22(GU) List of PADER Submissions Jan 2014 - Present , 7 pages
23(GU) List of Missed PADERs, 1 page
24(GU) Unplanned Deviation Report, Dated: 03/13/2017, 3 pages
25(GU) MedWatch 3500A Forms for Levofloxacin , 33 pages
26(GU) MedWatch 3500A Forms for Simvastatin , 37 pages
27(GU) MedWatch 3500A Forms for Sildenafil , 10 pages
28(GU) CIOMS Forms for Montelukast , 25 pages
29(GU) PADER Submission for Lamivudine Tablets 100 mg, Review Period: 12/29/2014 to 03/28/2015 , 3 pages
30(GU) PADER Submission for Simvastatin Tablets USP, Review Period: 02/24/2015 to 05/24/2015, 3 pages
31(GU) PADER Submission for Sildenafil Citrate Tablets, Review Period: 02/25/2015 to 05/25/2015, 3 pages
32(GU) PADER Submission for Lamivudine Tablets, Review Period: 03/29/2015 to 06/26/2015, 3 pages
33(GU) PADER Submission for Montelukast Sodium Tablets 10 mg, Review Period: 08/31/2016 to 11/28/2016, 3 pages
34(GU) Hetero USA SOP Index, 1 page
35(GU) Instructions for Handling Complaints received via Phone , 1 page
36(GU) Camber Pharmaceuticals SOP 23, Market Complaints, Effective Date: 01/13/2017 , 8 pages
37(GU) 2016 Quality Related Market Complaints , 4 pages
38(GU) Complaint MCU16-001 Finasteride Tablets 5 mg, 17 pages
39(GU) (b) (4) and Camber Service Agreement , 6 pages
40(GU) PADER Submission for Sildenafil Citrate Tablets, 20 mg, Review Period: 11/16/2017 to 02/13/2017, 2 pages
41(GU) PADER Submission for Entecavir Tablets, 0.5 mg and 1 mg, Review Period: 11/14/2016 to 02/11/2017, 3 pages
42(GU) Instructurion for Submission of PADERs by Hetero USA , 1 page
43(GU) FDA Compliance Leter, Dated: 10/06/2015, 2 pages
44(GU) DQRS Report for Esomeprazole Magnesium, Dated: 06/21/2016 , 3 pages
45(GU) 2016 Quarter II, ADR Market Complaint Logbook , 9 pages
46(GU) DQRS Report for Irbesartan, 150 mg, Dated: 03/15/2016 , 4 pages
47(GU) 2016 Quater I ADR Market Complaint Logbook , 14 pages
48(GU) DQRS Report for Valsartan 80 mg, Dated: 11/24/2015 , 4 pages
49(GU) 2015 Quarter V ADR Market Complaint Logbook, 9 pages
50(GU) 2016 Quater I ADR Market Complaint Logbook , 6 pages
51(GU) Regulatory Affairs Manager Job Description & Resume, #1, 5 pages
52(GU) Regulatory Affairs Job Description and Resume, #2, 8 pages
53(GU) Director of Regulatory Affairs Job Description & Resume , 4 pages

54(GU) (b) (4) Perfomance Qualification, Dated: 03/17/2017 , 7 pages
55(GU) Field Alert Report for Montelukast Sodium Tablets, 10 mg, Lot #MON16001B, 1 page

ATTACHMENTS
1(GU) Issued 483
2(GU) FDA-482, Notice of Inspection, 3 pages
3(GU) Hetero USA Inc. Assignment Memo , 8 pages

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